

SEQUENCE LISTING

<110> VERTEX PHARMACEUTICALS INC.

<120> METHODS AND COMPOSITIONS FOR RAPID DEVELOPMENT OF SCREENING ASSAYS

<130> VPI/02-143WO2

<140> PCT/US03/28078

<141> 2003-09-05

<150> 60/408,297

<151> 2002-09-05

<160> 86

<170> PatentIn version 3.2

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<212> DNA

<213> Escherichia coli

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<221> CDS

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<223> B-lactamase

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Gln Glu Gln Leu Gly Arg Arg Ile His Tyr Ser Gln Asn Asp Leu Val
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gag tac tca cca gtc aca gaa aag cat ctt acg gat ggc atg aca gta 288
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85 90 95

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				_		acg Thr				_	_				_		384
	u H					gat Asp											432
_	ŭ L	_		_	_	ata Ile 150			_		_	_		_	_		480
_	_		_	_		acg Thr	_	_						_			528
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_	a Ā					gcc Ala			_			_				_	672
	a L					ggt Gly 230											720
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	_	_	_		_	att Ile	_										795
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Le	u G	ly	Ala	Arg 20	Val	Gly	Tyr	Ile	Glu 25	Leu	Asp	Leu	Asn	Ser 30	Gly	Lys	
11	e L		Glu 35	Ser	Phe	Arg	Pro	Glu 40	Glu	Arg	Phe	Pro	Met 45	Met	Ser	Thr	
Ph	e L	ys	Val	Leu	Leu	Cys	Gly	Ala	Val	Leu	Ser	Arg	Val	Asp	Ala	Gly	

1

- Gln Glu Gln Leu Gly Arg Arg Ile His Tyr Ser Gln Asn Asp Leu Val Glu Tyr Ser Pro Val Thr Glu Lys His Leu Thr Asp Gly Met Thr Val 85 Arg Glu Leu Cys Ser Ala Ala Ile Thr Met Ser Asp Asn Thr Ala Ala Asn Leu Leu Thr Thr Ile Gly Gly Pro Lys Glu Leu Thr Ala Phe 120 Leu His Asn Met Gly Asp His Val Thr Arg Leu Asp Arg Trp Glu Pro Glu Leu Asn Glu Ala Ile Pro Asn Asp Glu Arg Asp Thr Thr Met Pro Ala Ala Met Ala Thr Thr Leu Arg Lys Leu Leu Thr Gly Glu Leu Leu 165 170 Thr Leu Ala Ser Arg Gln Gln Leu Ile Asp Trp Met Glu Ala Asp Lys Val Ala Gly Pro Leu Leu Arg Ser Ala Leu Pro Ala Gly Trp Phe Ile Ala Asp Lys Ser Gly Ala Gly Glu Arg Gly Ser Arg Gly Ile Ile Ala 215 Ala Leu Gly Pro Asp Gly Lys Pro Ser Arg Ile Val Val Ile Tyr Thr 230 Thr Gly Ser Gln Ala Thr Met Asp Glu Arg Asn Arg Gln Ile Ala Glu 250 Ile Gly Ala Ser Leu Ile Lys His Trp 260 <210> 3 <211> 858

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Asp	Arg	Trp	Glu	Pro 165	Glu	Leu	Asn	Glu	Ala 170	Ile	Pro	Asn	Asp	Glu 175	Arg	
Asp	Thr	Thr	Met 180	Pro	Ala	Ala	Met	Ala 185	Thr	Thr	Leu	Arg	Lys 190	Leu	Leu	
Thr	Gly	Glu 195	Leu	Leu	Thr	Leu	Ala 200	Ser	Arg	Gln	Gln	Leu 205	Ile	Asp	Trp	

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Ala Gly Trp Phe Il 225	e Ala Asp Lys 230	Ser Gly Ala Gly 235	y Glu Arg Gly	Ser 240
Arg Gly Ile Ile Al 24	_	Pro Asp Gly Lys 250	Pro Ser Arg 255	Ile
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Phe Lys Val Leu Leu 50	Cys Gly Ala 55	Val Leu Ser	Arg Asp Asp .	Ala Gly
Gln Glu Gln Leu Gly	Arg Arg Ile 70	His Tyr Ser 75	Gln Asn Asp	Leu Val 80

Glu	Tyr	Ser	Pro	Val 85	Thr	Glu	Lys	His	Leu 90	Thr	Asp	Gly	Met	Thr 95	Val	
Arg	Glu	Leu	Cys 100	Ser	Ala	Ala	Ile	Thr 105	Met	Ser	Asp	Asn	Thr 110	Ala	Ala	
Asn	Leu	Leu 115	Leu	Thr	Thr	Ile	Gly 120	Gly	Pro	Lys	Glu	Leu 125	Thr	Ala	Phe	
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Glu 145	Leu	Asn	Glu	Ala	Ile 150	Pro	Asn	Asp	Glu	Arg 155	Asp	Thr	Thr	Met	Pro 160	
Val	Ala	Met	Ala	Thr 165	Thr	Leu	Arg	Lys	Leu 170	Leu	Thr	Gly	Glu	Leu 175	Leu	
Thr	Leu	Ala	Ser 180	Arg	Gln	Gln	Leu	Ile 185	Asp	Trp	Met	Glu	Ala 190	Asp	Lys	
Val	Ala	Gly 195	Pro	Leu	Leu	Arg	Ser 200	Ala	Leu	Pro	Ala	Gly 205	Trp	Phe	Ile	
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Ala 225	Leu	Gly	Pro	Asp	Gly 230	Lys	Pro	Ser	Arg	Ile 235	Val	Val	Ile	Tyr	Thr 240	
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_		-	_				_		_	_	acc Thr	_	_		_	480
_	_	_		_	_	_					ggc Gly	-				528
											gag Glu					576
											ggc					624
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Lys Val Leu Leu Cys Gly Ala Val Leu Ser Arg Ile Asp Ala Gly Gln 50 55 60

Glu Gln Leu Gly Arg Arg Ile His Tyr Ser Gln Asn Asp Leu Val Glu 65 70 75 80

Tyr Ser Pro Val Thr Glu Lys His Leu Thr Asp Gly Met Thr Val Arg 85 90 95

Glu Leu Cys Ser Ala Ala Ile Thr Met Ser Asp Asn Thr Ala Ala Asn 100 105 110

Leu Leu Thr Thr Ile Gly Gly Pro Lys Glu Leu Thr Ala Phe Leu 115 120 125

His Asn Met Gly Asp His Val Thr Arg Leu Asp His Trp Glu Pro Glu 130 135 140

Leu Asn Glu Ala Ile Pro Asn Asp Glu Arg Asp Thr Thr Met Pro Val 145 150 155 160

Ala Met Ala Thr Thr Leu Arg Lys Leu Leu Thr Gly Glu Leu Leu Thr 165 170 175

Leu Ala Ser Arg Gln Gln Leu Ile Asp Trp Met Glu Ala Asp Lys Val 180 185 190

Ala Gly Pro Leu Leu Arg Ser Ala Leu Pro Ala Gly Trp Phe Ile Ala 195 200 205

Asp Lys Ser Gly Ala Gly Glu Arg Gly Ser Arg Gly Ile Ile Ala Ala 210 215 220

Leu Gly Pro Asp Gly Lys Pro Ser Arg Ile Val Val Ile Tyr Thr Thr 225 230 235 240

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ccg gat gag cgt ttt gct ttt gct tcg acg att aag gct tta act gta Pro Asp Glu Arg Phe Ala Phe Ala Ser Thr Ile Lys Ala Leu Thr Val 35 40 45	144
ggc gtg ctt ttg caa cag aaa tca ata gaa gat ctg aac cag aga ata Gly Val Leu Leu Gln Gln Lys Ser Ile Glu Asp Leu Asn Gln Arg Ile 50 55 60	192
aca tat aca cgt gat gat ctt gta aac tac aac ccg att acg gaa aag Thr Tyr Thr Arg Asp Asp Leu Val Asn Tyr Asn Pro Ile Thr Glu Lys 65 70 75 80	240
cac gtt gat acg gga atg acg ctc aaa gag ctt gcg gat gct tcg ctt His Val Asp Thr Gly Met Thr Leu Lys Glu Leu Ala Asp Ala Ser Leu 85 90 95	288
cga tat agt gac aat gcg gca cag aat ctc att ctt aaa caa att ggc Arg Tyr Ser Asp Asn Ala Ala Gln Asn Leu Ile Leu Lys Gln Ile Gly 100 105 110	336
gga cct gaa agt ttg aaa aag gaa ctg agg aag att ggt gat gag gtt Gly Pro Glu Ser Leu Lys Lys Glu Leu Arg Lys Ile Gly Asp Glu Val 115 120 125	384
aca aat ccc gaa cga ttc gaa cca gag tta aat gaa gtg aat ccg ggt Thr Asn Pro Glu Arg Phe Glu Pro Glu Leu Asn Glu Val Asn Pro Gly 130 135 140	432
gaa act cag gat acc agt aca gca aga gca ctt gtc aca agc ctt cga Glu Thr Gln Asp Thr Ser Thr Ala Arg Ala Leu Val Thr Ser Leu Arg 145 , 150 , 155 160	480

Ala Phe Ala	ctt gaa Leu Glu 165	_				_	_		_				528
atc gat tgg Ile Asp Trp	_	_					_	_			_	_	576
gga gcg gca Gly Ala Ala 195													624
cca aaa gga Pro Lys Gly 210		Val											672
aaa act gtt Lys Thr Val 225													720
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Thr Met Ala Asn Gly Gly Pro Leu Ala Phe Ser Phe Asp Ile Leu Ser 50 55 60

Thr Val Phe Lys Tyr Gly Asn Arg Cys Phe Thr Ala Tyr Pro Thr Ser 65 70 75 80

Met Pro Asp Tyr Phe Lys Gln Ala Phe Pro Asp Gly Met Ser Tyr Glu 85 90 95

Arg Thr Phe Thr Tyr Glu Asp Gly Gly Val Ala Thr Ala Ser Trp Glu
100 105 110

Ile Ser Leu Lys Gly Asn Cys Phe Glu His Lys Ser Thr Phe His Gly 115 120 125

Val Asn Phe Pro Ala Asp Gly Pro Val Met Ala Lys Lys Thr Thr Gly 130 135 140

Trp Asp Pro Ser Phe Glu Lys Met Thr Val Cys Asp Gly Ile Leu Lys 145 150 155 160

Gly Asp Val Thr Ala Phe Leu Met Leu Gln Gly Gly Gly Asn Tyr Arg 165 170 175

Cys Gln Phe His Thr Ser Tyr Lys Thr Lys Lys Pro Val Thr Met Pro 180 185 190

Pro Asn His Val Val Glu His Arg Ile Ala Arg Thr Asp Leu Asp Lys 195 200 205

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					ttc Phe											144
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Val Glu Gly Gly Pro Leu Pro Phe Ala Glu Asp Ile Leu Ser Ala Ala 50 55 60

Phe Asn Tyr Gly Asn Arg Val Phe Thr Glu Tyr Pro Gln Asp Ile Val 65 70 75 80

Asp Tyr Phe Lys Asn Ser Cys Pro Ala Gly Tyr Thr Trp Asp Arg Ser 85 90 95

Phe Leu Phe Glu Asp Gly Ala Val Cys Ile Cys Asn Ala Asp Ile Thr 100 105 110

Val Ser Val Glu Glu Asn Cys Met Tyr His Glu Ser Lys Phe Tyr Gly 115 120 125

Val Asn Phe Pro Ala Asp Gly Pro Val Met Lys Lys Met Thr Asp Asn 130 135 140

Trp Glu Pro Ser Cys Glu Lys Ile Ile Pro Val Pro Lys Gln Gly Ile 145 150 155 160

Leu Lys Gly Asp Val Ser Met Tyr Leu Leu Leu Lys Asp Gly Gly Arg 165 170 175

Leu Arg Cys Gln Phe Asp Thr Val Tyr Lys Ala Lys Ser Val Pro Arg 180 185 190

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Met	Asn 130	Phe	Pro	Ala		Gly 135				Lys	Lys 140	Met	Thr	Thr	Asn		
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Tyr	Arg	Cys	Gln 180	Phe	Asp	Thr	Val	Tyr 185	Lys	Ala	Lys	Ser	Val 190	Pro	Ser		
Lys	Met	Pro 195	Glu	Trp	His	Phe	Ile 200	Gln	His	Lys	Leu	Leu 205	Arg	Glu	Asp		

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gat tat cta aa Asp Tyr Leu Ly		_					
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ccg agc act ga Pro Ser Thr Gl 145						e Gly A	

	cat His															Ę	528
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	cac His															6	524
	atg Met 210															6	572
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ttg cag gat ggc t Leu Gln Asp Gly C 115	Cys Phe Ile			

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													cta Leu			52
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Phe Pro Ser Asp Gly Pro Val Met Gln Lys Lys Thr Met Gly Trp Glu 130 135 140	
Ala Ser Thr Glu Arg Leu Tyr Pro Arg Asp Gly Val Leu Lys Gly Glu 145 150 155 160	
Ile His Lys Ala Leu Lys Leu Lys Asp Gly Gly His Tyr Leu Val Glu 165 170 175	
Phe Lys Ser Ile Tyr Met Ala Lys Lys Pro Val Gln Leu Pro Gly Tyr 180 185 190	
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50 55 60	

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														aca Thr		:	336
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		_	_		_	_		_	_					gaa Glu		4	480
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_		_		_					_		_			atc Ile	_		720
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Thr Leu Arg Ile Pro Lys Ala Leu Thr Thr Met Gly Val Ile Lys Pro 35 40 45

Asp Met Lys Ile Lys Leu Lys Met Glu Gly Asn Val Asn Gly His Ala 50 55

Phe Val Ile Glu Gly Glu Gly Glu Gly Lys Pro Tyr Asp Gly Thr His 65 70 75 80

Thr Leu Asn Leu Glu Val Lys Glu Gly Ala Pro Leu Pro Phe Ser Tyr 85 90 95

Asp Ile Leu Ser Asn Ala Phe Gln Tyr Gly Asn Arg Ala Leu Thr Lys
100 105 110

Tyr Pro Asp Asp Ile Ala Asp Tyr Phe Lys Gln Ser Phe Pro Glu Gly
115 120 125

Tyr Ser Trp Glu Arg Thr Met Thr Phe Glu Asp Lys Gly Ile Val Lys 130 135 140

Val Lys Ser Asp Ile Ser Met Glu Glu Asp Ser Phe Ile Tyr Glu Ile 145 150 155 160

Arg Phe Asp Gly Met Asn Phe Pro Pro Asn Gly Pro Val Met Gln Lys
165 170 175

Lys Thr Leu Lys Trp Glu Pro Ser Thr Glu Ile Met Tyr Val Arg Asp 180 185 190

Gly Val Leu Val Gly Asp Ile Ser His Ser Leu Leu Leu Glu Gly Gly
195 200 205

Gly His Tyr Arg Cys Asp Phe Lys Ser Ile Tyr Lys Ala Lys Lys Val 210 215 220

Val Lys Leu Pro Asp Tyr His Phe Val Asp His Arg Ile Glu Ile Leu 225 230 235 240

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- Glu Gln Leu Phe Leu Leu Ile Phe Pro Arg Glu Asp Leu Asp Met Ile 65 70 75 80
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 85 90 95
- Phe Val Gln Asp Asn Val Asn Lys Asp Ala Val Thr Asp Arg Leu Ala
 100 105 110
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- Leu Asp Phe Met Pro Arg Asp Ala Leu His Gly Phe Asp Trp Ser Glu
 165 170 175
- Glu Asp Asp Met Ser Asp Gly Leu Pro Phe Leu Lys Thr Asp Pro Asn 180 185 190
- Asn Asn Gly Phe Phe Gly Asp Gly Ser Leu Leu Cys Ile Leu Arg Ser
- Ile Gly Phe Lys Pro Glu Asn Tyr Thr Asn Ser Asn Val Asn Arg Leu 210 215 220
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- Ser Arg Leu Leu Gln Ser Tyr Leu Asn Asn Phe His Pro Tyr Cys Pro 245 250 255
- Ile Val His Ser Pro Thr Leu Met Met Leu Tyr Asn Asn Gln Ile Glu 260 265 270
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- Ile Gly Ala Trp Cys Ile Glu Gly Glu Ser Thr Asp Ile Asp Val Phe 290 295 300
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- Gly Ser Ile Ile Leu Val Thr Ala Leu His Leu Leu Ser Arg Tyr Thr 325 330 335
- Gln Trp Arg Gln Lys Thr Asn Thr Ser Tyr Asn Phe His Ser Phe Ser 340 345 350
- Ile Arg Met Ala Ile Ser Leu Gly Leu Asn Arg Asp Leu Pro Ser Ser 355 360 365
- Phe Ser Asp Ser Ser Ile Leu Glu Gln Arg Arg Ile Trp Trp Ser 370 375 380
- Val Tyr Ser Trp Glu Ile Gln Leu Ser Leu Leu Tyr Gly Arg Ser Ile 385 390 395 400
- Gln Leu Ser Gln Asn Thr Ile Ser Phe Pro Ser Ser Val Asp Asp Val
 405 410 415
- Gln Arg Thr Thr Gly Pro Thr Ile Tyr His Gly Ile Ile Glu Thr 420 425 430
- Ala Arg Leu Leu Gln Val Phe Thr Lys Ile Tyr Glu Leu Asp Lys Thr 435 440 445
- Val Thr Ala Glu Lys Ser Pro Ile Cys Ala Lys Lys Cys Leu Met Ile 450 455 460
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- Met Asp Ile Ser Thr Thr Ala Leu Thr Asn Leu Leu Lys Glu His Pro 485 490 495
- Trp Leu Ser Phe Thr Arg Phe Glu Leu Lys Trp Lys Gln Leu Ser Leu
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- Asn Cys Ser Tyr Tyr Leu Phe Asn Ala Val Leu Val Pro Ile Lys Thr 580 585 590
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- Leu Leu Gln Gln Ile Asn Thr Val Leu Met Leu Leu Lys Lys Leu Ala 610 615 620

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Leu	. Arg	Val	Ser	Gly	Met	Ser	Met 120	Lys	Asp	Ile	Gly	11e	Met	Asp	Gly
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Val		. Ala	a Arç	, Ile	2 Asp	As <u>r</u>	Glu	ı Val	Thi	val 155	Lys	arg	J Leu	Lys	160
Glr	ı Gly	y Ası	ı Lys	Val	Glu 5	ı Leı	ı Lev	ı Pro	Glu 170	Ası O	ı Sei	c Glu	ı Phe	Lys 175	Pro
Ile	e Va	L Va	l Asp 180	p Let	ı Arç	g Gli	n Glr	n Ser 18	r Phe	e Thi	r Ile	e Glu	1 Gly 190	, Let	ı Ala
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<223> any purine

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<213> Artificial Sequence

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<213> Artificial Sequence

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